

**Chiral Problems?** 



**Cover Story** 

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# **Out Of The Ivory Tower**

### Ionic liquids are starting to leave academic labs and find their way into a wide variety of industrial applications

#### Patricia L. Short

For years, ionic liquids have been the darlings of academia, where researchers have explored the chemistry and properties of this class of low-melting-point salts. The range of properties of ionic liquids, including nonvolatility and nonflammability, is particularly appealing.



**BASF** Photo

Small Scale Veit Stegmann examines the result of a phase separation resulting from BASF's BASIL process.

Now, after a fitful start, commercial applications are beginning to appear. And those applications are increasingly sophisticated, according to Uwe Vagt, in global new business development for <u>BASF</u>'s chemical intermediates and special technologies unit.

In 1980, Vagt notes, there were only a few patent applications for ionic liquids. In 2000, there were nearly 100 applications, and by 2004, more than 800. "We have moved from pure academia to commercial topics," he says. "But we are still in a very early stage."

At the same time as they develop new products, companies are coming to grips with the commercial reality of product registrations for materials used in quantities larger than lab-scale. Companies are shaping their strategies for selecting cations and anions for ionic liquids, making the best use of existing data to ease the newproduct-registration process.

The key to ionic liquids is that most are fluids at less than 100 <sup>o</sup>C. Bernd Weyershausen, global marketing manager for <u>Degussa's</u> <u>Goldschmidt Industrial Specialties</u> unit, explains that liquidity is achieved by tailoring cations and anions to disturb a salt's normally highly crystalline nature. For example, sodium chloride, the archetypal salt, has a melting point of just over 800 <sup>o</sup>C. The melting point of ionic liquid imidazolium chloride, by contrast, is 80 <sup>o</sup>C,

thanks to the replacement of sodium with a bulky cation.

Choice of cation or anion can also affect other salt properties, including density, viscosity, and water stability and miscibility.

Tailor-made ionic liquids are becoming increasingly important, and long gone are the days of simply taking a compound off the shelf and hoping it will work. As Philip E. Rakita, managing director of Philadelphia-based industry consultant <u>Armour Associates</u>, points out, given the wide variety of cations and anions that can make up ionic liquids, there are "virtually unlimited permutations" for a researcher to use in compound design.



The wide slate of potential liquids, in turn, has opened the door to new applications beyond the early suggestion of ionic liquids as nonpolluting "green" solvents that could replace volatile organic compounds. One area of research depends upon the liquids' electrochemical properties, with some work on ionic liquids as battery electrolytes going back to the early 1980s.

Most of the applications that do come to fruition will be relatively small, Rakita predicts. "Everybody is looking for the blockbuster but it won't happen. There will be \$1 million here and \$5 million there, a lot of different uses in a lot of different markets." He predicts that the worldwide ionic liquids business could add as much as \$50 million annually "in a very short time. But that is adding up a lot of little uses, with no single player being dominant."

Rakita adds that the size of the market is relative. For many small companies in the field, he points out, a market worth \$1 million per year is exciting. However, large companies in the arena, such as BASF, Degussa, Merck, and Cytec Industries, have different scales for success. "Someone in each of those companies is saying, 'There's a project in my plans that will have sales of \$10 million or \$20 million per year eventually,' " Rakita observes.

Sales projections are understandably still vague in a business that

is less than a decade old. Most industry observers reckon that the chemical industry's interest in ionic liquids was kick-started only in 1999 by <u>Solvent Innovation</u>, founded in Cologne, Germany.

The company, in which Degussa has taken a small investment stake, was formed almost out of desperation by scientists at <u>Germany's Aachen University of Technology</u>. Working with oil and chemical giant <u>BP</u>, chemist <u>Peter Wasserscheid</u> and his team at Aachen were exploring the impact of placing polymerization catalysts in ionic liquids.

"We were bothered by companies wanting samples of ionic liquids. It was just too much," says Claus Hilgers, president and chief executive officer of Solvent Innovation, who was earning his Ph.D. at Aachen at the time. Talks with industry professionals indicated that people wanted the ionic liquids and were willing to pay for them, he recalls, so the company was formed to supply them in kilogram quantities.

The industry's concept of what ionic liquids can do has evolved significantly since then, Hilgers says. "There are a lot of applications, starting as a replacement for solvents. But we are now in advanced materials and functional compounds. That is the direction where we see the future, rather than classical chemistry." Other market possibilities, he says, include high-performance lubricants, compressor fluids, and dispersion of nanoparticles in various kinds of matrices.

"The unique properties of ionic liquids are solving problems. At least that's what we're doing," Hilgers says. "We've seen some interesting ideas. Some have been fairly strange, but many have worked out. The industry has become a little more grown-up."

Solvent Innovation has grown up as well. "We are a systems solution provider in ionic liquids," Hilgers says. "We started with supplying, and now we offer the complete portfolio of customer services: joint development, consultancy, and so on. We support our customers and help them to be more successful. Just supplying new technology is not sufficient."

The company has the capacity to produce 20 metric tons of ionic

liquids per year, he says. "We could extend up to 50 or 100 metric tons, but that's it. We won't go beyond that. We are positioned between the global players and the small guys." If his company needs significantly larger quantities, he adds, it would work with Degussa, BASF, or another large company to actually produce the compounds.

Indeed, such chemical giants are at the opposite end of the corporate spectrum in ionic liquids. BASF entered the field in 2002, Vagt says, with a process it calls BASIL, which stands for biphasic acid scavenging utilizing ionic liquids. Developed by new business development team member Matthias Maase, the process went live in October 2004 as part of a new route to precursors for photoinitiators that are used in UV-curable coatings.

The BASIL process yields the photoinitiator precursor alkoxyphenylphosphine and the ionic liquid *N*-methylimidazolium chloride. The ionic liquid is easily separated, then washed with sodium hydroxide to recycle the imidazole. The new process, Vagt points out, uses a very small reactor rather than the large one used previously; yield is increased by a factor of 10<sup>4</sup>. BASF is using the process in other syntheses and has licensed it to other companies. For example, Germany's Schering began using the BASIL process for drug synthesis at one of its sites early last year.

BASF is now looking for other applications where ionic-liquid technology can help. At least two processes are in the pilot stage.

One is a route to chlorinated alcohols that replaces a phosgenebased route. The new process, which employs hydrochloric acid and an ionic liquid, will go into commercial-scale production by the middle of this year, Vagt says. Since early spring, BASF also has been running a pilot-scale extractive distillation using an ionic liquid as an entrainer, or separation enhancer. This approach significantly cuts the costs of separation and recycling of the entrainer, he claims

Vagt is particularly enthusiastic about using ionic liquids to process cellulosic materials. Cellulosics form stable solutions in ionic liquids, he says; cellulose can then be regenerated through precipitation by the addition of water, methanol, or propyl alcohol.

PUT TO USE Ionic liquids are being developed for a wide variety of applications		
Analytics	Electrochemistry	Engineering Fluids
Gas chromatography	Electrolyte in batteries	Lubricants
columns	Electrolyte in sensors	Thermodynamic fluids
Stationary phase for	Metal plating	
high-performance liquid		Performance Additives
chromatography	Synthesis	Plasticizers
Matrices for mass spec-	Solvents	Dispersing agents
trometry	Catalysis	Compatibilizers
-	Biphasic reactions	Solubilizers
Separation	Manufacture of nanoma-	
Gas absorption	terials	
Extraction	Microwave chemistry	SOURCE- Deguissa

**The technology** could, for example, be harnessed to produce cellulosic fibers in an environmentally benign process, replacing the currently used viscose process, which relies on carbon disulfide as a processing solvent.

Last month, BASF and the <u>University of Alabama</u> formalized a license and cooperative agreement giving BASF exclusive rights to patents covering the use of ionic liquids to dissolve, regenerate, and process cellulose. "This technology enables us to produce blends or polymers and cellulose that provide excellent plastics performance,' says <u>Robin D. Rogers</u>, chemistry professor and director of the university's <u>Center for Green Manufacturing</u>. Among the possibilities: packaging film blends of cellulose and polypropylene that have exceptional tear strength, and encapsulation of pharmaceutical or crop protection ingredients together with magnetic particles to provide focused treatments.

And at least one similar process has been demonstrated on silk fibers, opening up the possibility of enhancing or tailoring the properties of silk.

The solvent properties of ionic liquids also come into play at the start-up company <u>Bioniqs</u>, although in the somewhat more specialized field of biocatalysis. Adam Walker, chief scientific officer, explains that the roots of the company go back to 2000, when he was working on his Ph.D. in biocatalysis with <u>Neil Bruce</u> at the University of Cambridge's department of chemistry.

"One of the problems I had was that my enzymes were subject to hydrolysis, but redox enzymes don't work in organic solvents," he recalls. He tried using the more commonly available imidazolium ionic liquids as solvents, but found that they didn't work. So he went back to basics: To work, the enzymes needed an environment with the properties of water. "So we designed an ionic liquid that would mimic water," Walker says, but would not hydrolyze enzymes.

Bruce moved to the <u>University of York</u> to become a professor of biotechnology, and Walker followed him there for his postdoc. With funding from the U.K.'s <u>Pro-Bio Faraday</u> plan, Walker looked at how ionic liquids could be commercialized for use as biocatalysis solvents. This work led to the development of what he terms simple ionic liquids, produced by neutralizing selected amines.

Bioniqs was formed in December 2004 with funding from the University of York; <u>Amaethon</u>, the university's corporate development body; and venture capitalists <u>IP2IPO</u>. It focuses on three core areas: biology and biotechnology, natural product extraction, and reactor cleaning and decontamination.

"We have just completed a process for the extraction from a natural product of an antimalarial drug," Walker says. "And we have done quite a lot of work into tailor-made ionic liquids for dissolving poorly soluble active pharmaceutical ingredients off the walls of reactors. These kinds of applications would be serious scale—multiton."

Walker concedes that demand of that magnitude would swamp any capacity Bioniqs has. "We can't do anything over 1 kg, realistically," he says. The need for larger quantity capabilities led, in February, to an agreement with Germany's Merck, which is already in the ionic liquids business as an offshoot of its liquid-crystal expertise.

Merck will provide Bioniqs with scale-up capability and will add Bioniqs' ionic liquids to the Merck laboratory chemicals catalog for general distribution. Walker adds, "We think we can develop tailormade ionic liquids at a competitive price."

Meanwhile, at Degussa's Goldschmidt unit, the focus of market development has turned to exploiting the functional properties of ionic liquids.

According to Weyershausen, the company began synthesizing ionic liquids several years ago and now markets R&D quantities through

Solvent Innovation. But Goldschmidt also has already developed some applications, he says. "We are selling ionic liquids to our customers as performance additives such as dispersing agents in paints and inks," he says.

He cites interest in developing ionic liquids as potential replacements for mineral oils and synthetic lubricants. Because of their chemical nature, ionic liquids have different properties that could benefit lubricants, Weyershausen suggests.

On the other hand, he cautions that "every time you think of an application, there will be drawbacks as well." For example, a lubricant formulator seeking to substitute an ionic liquid for a minera oil might encounter compatibility problems with sealants that have been developed to work with mineral oil. "This technology is not a panacea," Weyershausen says.



Degussa Photo

**Getting Bigger** 

Degussa's process technology unit scales up ionic liquids for industrial uses. **High costs**, however, are probably surmountable. "The price might look bad in the beginning, but it is always price-to-performance that is important," he points out. If the performance of an ionic liquid is 20 times that of the material it aims to replace, for example, a customer would need much less of the ionic liquid.

"You always need to help a customer differentiate a product from a competitors' or make a technology leap," Weyershausen says. "If the improvement is only incremental, you'd better forget about it."

Weyershausen is quick to dampen expectations arising from early research into ionic liquids, particularly when it comes to predictions of widespread applicability. "Most of the ionic liquids that academia is playing with are new chemicals. They are not listed," he points out. They can be used in research but can't be used in large quantities without being registered with the authorities around the world. And that, Weyershausen adds, involves considerable amounts of time and money.

"In Degussa," he says, "researchers have some degree of freedom to work on potential projects and to be innovative. But once something becomes a bigger, controlled project, questions come up: Toxicity? Raw materials? Availability? Listing? These questions do kill some projects."

It's a chicken-and-egg situation, he adds. Companies won't develop a compound, manufacture it, and go to the expense of registering it, just in the hope that an application can be found. On the other hand customers are reluctant to develop applications for compounds that have not yet been registered.

One factor that does help with the new product registration process, Vagt says, is that the toxicology and ecotoxicology of an ionic liquid will mainly depend on the cations. By judiciously choosing the cations, in particular, he suggests, "the effort to get some of the analogs listed will be less."

"For any application, we try to talk with companies about materials already registered. But if those aren't appropriate for the customer's problem," Hilgers says, "we develop other materials. We tell the customer it will be about six to nine months for full registration and that cost will be included in the development costs."

In a field as young as ionic liquids, rampant new product development is going to be a fact of life. According to Vagt, the ionic liquid that fulfills all requirements "doesn't exist. You need to define the properties you want, then design the compound that is best for those properties."

He concedes that the field has seen quite a bit of hype, but says, "That's not necessarily bad—it gets people interested. You especially need that in the performance chemicals field. As more information on this topic gets around, it gets people to think about the concept of ionic liquids."

In the early days of ionic liquids, Hilgers recalls, it was always a drawback that the research was just academic. Academic research "supports us, and we are glad for that, but there is a change now. There is a business behind this science, and people are making money from it."

#### Cover Story - Ionic Liquids

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### IUPAC Project Aims To Plug Ionic Liquids Data Gap

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